Cancer Chemother Pharmacol (2012) 70:489
DOI 10.1007/s00280-012-1928-5

REPLY TO THE LETTER

In response

Masashi Kanai · Shigemi Matsumoto · Yoshihiko Otsuka · Masafumi Fukuda · Atsushi Imaizumi

Received: 7 February 2012 / Accepted: 22 May 2012 / Published online: 29 July 2012

We greatly appreciate the interest of Gescher et al. in our manuscript and the opportunity to respond to their correspondence. We understand their concerns that our study did not present levels of parent curcumin, which is considered to play a major role of anticancer effects of this agent.

We observed in a rat model that Theracurmin® could increase the parent curcumin level as well as conjugated curcumin level (unpublished data). Unfortunately, however, we could not detect parent curcumin levels in human subjects after administration of 210 mg of Theracurmin® or 8 g of unformulated curcumin manufactured by Sabinsa Corporation (Piscataway, NJ, USA), which were also used in other clinical trials [2, 3]. We believe that the parent curcumin level in our study was less than 0.5 ng/mL, which is the lower limit of detection in our LC-MSMS system. Supporting our observation, Vareed et al. [5] reported that they failed to detect parent curcumin levels even after administration of 12 g of Sabinsa curcumin. Similarly, Garcea et al. [1] could detect only trace amounts of parent curcumin after the administration of 3.6 g of Sabinsa curcumin.

On the other hand, several researchers have proposed that conjugated curcumin can show its activity after deconjugation at the target sites [5] and that conjugated curcumin itself has some important biological functions [4].

Therefore, we believe that an increase in conjugated curcumin levels achieved by Theracurmin® can potentially improve the efficacy of this agent in human subjects, and several clinical trials are now underway to verify this hypothesis.

M. Kanai (✉) · S. Matsumoto
Department of Clinical Oncology and Pharmacogenomics, Graduate School of Medicine, Kyoto University, 54 Shogoin Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan
e-mail: kanai@kuhp.kyoto-u.ac.jp

Y. Otsuka · M. Fukuda · A. Imaizumi
Theravalues Corporation, 3-12, Kioicho Chiyoda-ku, fTokyo 102-0094, Japan

References

1. Garcea G, Berry DP, Jones DJ, Singh R, Dennison AR, Farmer PB, Sharma RA, Steward WP, Gescher AJ (2005) Consumption of the putative chemopreventive agent curcumin by cancer patients: assessment of curcumin levels in the colorectum and their pharmacodynamic consequences. Cancer Epidemiol Biomarkers Prev 14:120–125
2. Kanai M, Imaizumi A, Otsuka Y, Sasaki H, Hashiguchi M, Tsujiko K, Matsumoto S, Ishiguro H, Chiba T (2011) Dose-escalation and pharmacokinetic study of nanoparticle curcumin, a potential anticancer agent with improved bioavailability, in healthy human volunteers. Cancer Chemother Pharmacol 69: 65–70
3. Kanai M, Yoshimura K, Asada M, Imaizumi A, Suzuki C, Matsumoto S, Nishimura T, Mori Y, Masui T, Kawaguchi Y, Yanagihara K, Yazumi S, Chiba T, Guha S, Aggarwal BB (2010) A phase I/II study of gemcitabine-based chemotherapy plus curcumin for patients with gemcitabine-resistant pancreatic cancer. Cancer Chemother Pharmacol 68:157–164
4. Pfeiffer E, Hoehle SI, Walch SG, Riess A, Solyom AM, Metzler M (2007) Curcuminoids form reactive glucuronides in vitro. J Agric Food Chem 55:538–544
5. Vareed SK, Kakarala M, Ruffin MT, Crowell JA, Normolle DP, Djuric Z, Brenner DE (2008) Pharmacokinetics of curcumin conjugate metabolites in healthy human subjects. Cancer Epidemiol Biomarkers Prev 17:1411–1417